

IN THE CLAIMS:

1. (Currently amended) A method of identifying at least one of a plurality of preselected polymorphisms that may be present in a cytochrome P450 2D6 gene sequence in a sample, the method comprising:

(a) incubating a reaction comprising:

(i) an amount of nucleic acid obtained from said sample sufficient for primer extension, wherein said nucleic acid comprises said P450 2D6 gene sequence,

(ii) a nucleic acid polymerase,

(iii) a plurality of extension primers that specifically bind to a P450 2D6 gene sequence, and that, when extended by one nucleotide at the 3' end, comprise a nucleotide indicative of one of a plurality of preselected polymorphisms in said P450 2D6 gene sequence, and

(iv) a set of distinctively labeled ddNTPs,

under conditions such that at least one of said extension primers is distinctively labeled by addition of one of said labeled ddNTPs ~~comprising a label~~ to the [[5']] 3'-end of said at least one of said detection extension primers, to generate at least one labeled nucleic acid corresponding to at least one of said preselected polymorphisms; and

(b) using said at least one labeled nucleic acid to identify the said at least one of a plurality of preselected polymorphisms present in a cytochrome P450 2D6 gene sequence in the nucleic acid sample relating the labeled nucleic acid to the identity of said polymorphism in said sample.

2. (Original) The method of claim 1, wherein said nucleic acid is obtained from said sample by amplification of DNA in said sample.

3. (Currently amended) The method of claim 2, wherein said ~~amplification is accomplished by the addition of~~ **plurality of extension primers comprises** nucleic acid primers having SEQ ID NOs 1 to 8.

4. (Currently amended) The method of claim 1, wherein said **using** ~~[[relating]]~~ step (b) comprises mobilizing said **at least one** labeled nucleic acid~~[[s]]~~ by electrophoresis.

5. (Original) The method of claim 4, wherein said electrophoresis is capillary electrophoresis.

6. (Currently amended) The method claim 1, wherein one or more of steps (a) ~~[[,]]~~ **or (b) or (c), or combinations thereof,** are automated.

7. (Original) The method of claim 1, wherein said distinctive labeled ddNTPs are fluorescently labeled.

8. (Currently amended) The method of claim 1, wherein said **one of a** plurality of preselected **polymorphisms in said cytochrome P450 2D6 gene sequence is** ~~polymorphisms~~ **are independently** selected from the group consisting of a duplication, a deletion, an inversion, an insertion, a translocation, a polymorphism resulting in aberrant RNA splicing, and a single nucleotide polymorphism.

9. (Original) The method of claim 1, wherein said preselected cytochrome P450 2D6 polymorphisms are selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.

10. (Original) The method of claim 9, wherein said extension primers have sequences selected from the group consisting of SEQ ID NOS: 9 through 19.

11. (Original) The method of claim 1, wherein said sample is a human sample.

12. (Currently amended) The method of claim 1, wherein said **one of a plurality of** polymorphisms is associated with phenotype selected from the group consisting of having a reduced rate or degree of metabolism of one or more xenobiotics or endobiotics, an increased

rate or degree of metabolism of one or more xenobiotics or endobiotics, a decreased or increased specificity for one or more xenobiotics or endobiotics, and combinations thereof.

13. (Currently amended) The method of claim 12, wherein said one or more xenobiotics is a toxin, a carcinogen or a narcotic, or a metabolic precursor thereof.

14. (Original) The method of claim 13, wherein said sample is a sample from a subject having a genetic predisposition to suffer from a toxin, a carcinogen, or a narcotic.

15. (Currently amended) The method of claim 12, wherein said one or more xenobiotics is a therapeutic drug or a metabolic precursor thereof.

16. (Original) The method of claim 15, wherein said therapeutic drug is a cardioactive drug or a psychoactive drug.

17. (Original) The method of claim 15, wherein said subject has a disease or disorder that may be treated by said therapeutic drug.

18. (Original) The method of claim 1 further comprising detection of wildtype P450 2D6.

19. (Currently amended) A method of identifying [[a]] at least one polymorphism in a cytochrome P450 2D6 gene sequence in a sample, the method comprising:

identifying said at least one polymorphism by nucleotide primer extension conducted in a single reaction comprising nucleic acid from the sample, a plurality of extension primers for a plurality of cytochrome P450 2D6 gene polymorphisms, wherein the extension primers for each polymorphism differ in length from each other, and distinctively labeled ddNTPs;

generating at least one labeled extension primer by primer extension with the distinctively labeled ddNTP

subjecting the labeled extension primers to a size separation method, and

using the length of the labeled extension primer and the identity of its distinctively labeled ddNTP to identify at least one polymorphism in a cytochrome P450 2D6 gene sequence in a sample

~~generating from said sample a labeled nucleic acid comprising a means for distinguishing amongst a plurality of preselected polymorphisms in said P450 2D6 gene; and~~

~~relating said labeled nucleic acid to the identity of said polymorphism in said sample.~~

20. (Currently amended) The method of claim 19, wherein said nucleic acid from the sample is obtained ~~from said sample~~ by amplification of DNA in said sample.

21. (Currently amended) The method of claim 20, wherein said amplification is ~~accomplished by~~ comprises the addition of nucleic acid primers having SEQ ID NOs 1 to 8.

22. (Currently amended) The method of claim 19, wherein said step of subjecting the labeled extension primers to a size separation method is achieved ~~means for distinguishing amongst a plurality of preselected polymorphisms comprises a primer extension reaction with distinctively labeled ddNTPs and size separation of labeled primers~~ by electrophoresis.

23. (Original) The method of claim 22, wherein said electrophoresis is capillary electrophoresis.

24. (Currently amended) The method claim 19, wherein said step of subjecting the labeled extension primers to a size separation method ~~means for distinguishing amongst a plurality of preselected polymorphisms~~ is automated.

25. (Original) The method of claim 22, wherein said distinctively labeled ddNTPs are fluorescently labeled.

26. (Currently amended) The method of claim 19, wherein said plurality of preselected cytochrome polymorphisms in said P450 2D6 gene ~~polymorphisms~~ are

independently selected from the group consisting of a duplication, a deletion, an inversion, an insertion, a translocation, a polymorphism resulting in aberrant RNA splicing, and a single nucleotide polymorphism.

27. (Currently amended) The method of claim 19, wherein said preselected cytochrome **polymorphisms in said** P450 2D6 **gene polymorphisms** are selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.

28. (Currently amended) The method of claim 27, wherein said extension primers have sequences selected from the group consisting of **comprises** SEQ ID NOS: 9 through 19.

29. (Original) The method of claim 19, wherein said sample is a human sample.

30. (Original) A method of selecting a therapeutic drug, or a prodrug thereof, to treat a subject suffering from a disease or disorder, said method comprising:

selecting said therapeutic drug or prodrug to be compatible with a cytochrome P450 2D6 genotype of said subject identified by the method of claim 1 or 19.

31. (Original) A method of selecting a dosage of a therapeutic drug, or a prodrug thereof, to treat a subject suffering from a disease or disorder, said method comprising:

selecting said dosage to be compatible with a cytochrome P450 2D6 genotype of said subject identified by the method of claim 1 or 19.

32. (Currently amended) The method of claim 31 **[[or 32]]**, wherein said P450 2D6 genotype of said subject comprises a cytochrome P450 2D6 gene selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.

33. (Withdrawn) A substantially purified nucleic acid that hybridizes to the P450 2D6 gene, said nucleic acid selected from the group consisting of SEQ ID NOs 9 to 19.

34. (Withdrawn) The substantially purified nucleic acid of claim 33 wherein said nucleic acid is SEQ ID NO:11.

35. (Withdrawn) The substantially purified nucleic acid of claim 33 wherein said nucleic acid is SEQ ID NO:14.

36. (Currently amended) A method of identifying at least one of a preselected polymorphism that may be present in a cytochrome P450 2D6 gene sequence in a human sample, the method comprising:

(a) incubating a reaction comprising:

(i) an amount of nucleic acid obtained from said sample sufficient for primer extension, wherein said nucleic acid comprises said P450 2D6 gene sequence,

(ii) a nucleic acid polymerase,

(iii) at least one extension primer selected from the group consisting of SEQ ID NOs 9 to 19, and

(iv) a set of distinctively labeled ddNTPs,

under conditions such that said at least one extension primer is distinctively labeled by addition of one of said distinctively labeled ddNTPs comprising a label to the [[5']] 3'-end of said at least one ~~detection~~ extension primer, to generate at least one labeled nucleic acid corresponding to at least one of said preselected polymorphisms; and

(b) using said at least one labeled nucleic acid to identify the said at least one of a plurality of preselected polymorphisms present in a cytochrome P450 2D6 gene sequence in the nucleic acid sample ~~relating the labeled nucleic acid to the identity of said polymorphism in said sample.~~

37. (Original) The method of claim 36, wherein said nucleic acid is obtained from said sample by amplification of DNA in said sample.

38. (Currently amended) The method of claim 37, wherein said ~~amplification is accomplished by the addition of~~ plurality of extension primers comprises nucleic acid primers having SEQ ID NOs 1 to 8.

39. (Currently amended) The method of claim 36, wherein said using ~~relating~~ step (b) comprises mobilizing said at least one labeled nucleic acid~~[(s)]~~ by electrophoresis.

40. (Original) The method of claim 39, wherein said electrophoresis is capillary electrophoresis.

41. (Currently amended) The method claim 36, wherein one or more of steps (a)~~[(,)]~~ or (b) or (c), or combinations thereof, are automated.

42. (Original) The method of claim 36, wherein said distinctive labeled ddNTPs are fluorescently labeled.

43. (Withdrawn) The method of claim 36, wherein said primers are SEQ ID NO: 17, 18 and 19.

44. (Currently amended) The method of claim 36, wherein said extension primer~~[[s are]]~~ is SEQ ID NO: 11.

45. (Currently amended) The method of claim 36, wherein said extension primers are SEQ ID NO: 11 and ~~[[ND]]~~ 14.

46. (New) The method of claim 30, wherein said P450 2D6 genotype of said subject comprises a cytochrome P450 2D6 gene selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.